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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,060	02/12/2002	David Mu	38002-0024	2406

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,060	MU ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,9-14,22-24 and 33-35* is/are pending in the application.

4a) Of the above claim(s) *4-8, 15-21, 25-32 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,9-14,22-24 and 33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is a response to the Election filed October 27, 2003.

Claims 1-38 are pending in the instant application.

Claims 4-8, 15-21, 25-32 and 36-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement on October 27, 2003

Claims 1-3, 9-14, 22-24 and 33-35 have been examined on the merits.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-3, 9-14, 22-24 and 33-35) is acknowledged. The traversal is on the ground(s) that Group V (claims 25-31) should be examined with the elected invention since it should not be a serious burden for the Examiner to examine these claims as well.

Applicant's arguments have been considered but are not found persuasive because the inventions of Groups I and V are distinct each from the other. Group V (claims 25-31) is drawn to an isolated hepsin gene amplicon. The invention of Group V is related to the invention of Group I as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the products can be used in materially different processes of use. For example, the isolated hepsin

gene amplicon of Group V can be used as a nucleotide molecule that inhibits hepsin gene function, which is a materially different process than a method for diagnosing a cancer in a mammal, comprising detecting and measuring the hepsin gene copy number and expression in a subject, as in Group I. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter and because the searches required for the groups are not co-extensive, restriction for examination purposes as indicated is proper. Regarding the burden of search, the claims of Groups I and V are classified differently, necessitating different searches in the U.S. Patent databases. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group.

For these reasons, the restriction requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The Information Disclosure Statements, filed November 4, 2002 and June 17, 2002 are acknowledged. The references referred to therein have been considered on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 9-11, and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-3 and 9-11 are drawn to a method for diagnosing a cancer or monitoring therapeutic efficacy in a mammal comprising measuring hepsin gene copy number in a biological subject from a region that is cancerous and comparing the hepsin copy number to a control, wherein the biological subject is selected from ovarian, prostate, breast, or lung tissue. Claims 22-24 are drawn to a method of monitoring therapeutic efficacy in a mammal comprising measuring hepsin mRNA expression levels in a biological subject from a region that is cancerous and comparing the hepsin mRNA transcript to a control, wherein the biological subject is selected from ovarian, prostate, breast, or lung tissue.

The instant specification teaches TaqMan epicenter data for hepsin and provides methodologies for differential sensitivity of ovarian cancer cells to hepsin antibodies *in vitro*.

The instant Specification, at page 4, lines 19-31 teaches the activity of hepsin as an extracellular protease implicated as having a potential role in tumor progression. Page 4, lines 19-31 further teaches the disclosure of Tanimoto et al. Cancer Research, 1997 Vol. 57:2994-2887) who determined the level of expression of the hepsin gene in ovarian carcinomas and ovarian tumors compared to normal ovarian tissue is frequently over expressed. However, the instant Specification provides no correlation between hepsin gene copy number and cancer diagnosis or therapeutic efficacy as contemplated in claims 1-3 and 9-11. Further, the

Specification provides no correlation between hepsin expression and therapeutic efficacy as contemplated in claims 22-24. Without a correlation between hepsin gene copy number and cancer diagnosis or therapeutic efficacy, the skilled artisan would not be able to practice the instant invention without undue experimentation. Similarly, without a correlation between hepsin expression and therapeutic efficacy, the skilled artisan would not be able to practice the invention without undue experimentation.

The first issue is whether hepsin gene copy number correlates with treatment efficacy. For example, one gene copy over expressing may indicate the treatment is not efficacious, but if the assay only looks at gene copy number, it would provide a false result. The second issue is whether hepsin expression correlates with treatment efficacy. For example, other protein expression levels be lowered, indicating efficacy of treatment, hepsin unchanged, and this would be a false negative.

The Specification does not provide adequate guidance for one of skill to determine the correlation between hepsin gene copy number and cancer diagnosis and therapeutic efficacy to practice the instant invention. Without a correlation between hepsin gene copy number and cancer diagnosis and therapeutic efficacy, one of skill in the art would be required to perform undue trial and error experimentation. Similarly, the Specification does not provide adequate guidance for one of skill to determine the correlation between hepsin mRNA expression and therapeutic efficacy to practice the instant invention. The Specification does not enable a method for diagnosing a cancer in a mammal comprising measuring hepsin gene copy number in a biological subject from a region that is cancerous and comparing the hepsin gene copy number to a control, wherein the biological subject is selected from ovarian, prostate, breast, or lung

tissue or a method of monitoring the efficacy of a therapeutic treatment regimen in a patient comprising measuring hepsin gene copy number or hepsin mRNA expression levels in a biological subject from a region that is cancerous and comparing the hepsin gene copy number or the hepsin mRNA transcript to a control, wherein the biological subject is selected from ovarian, prostate, breast, or lung tissue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Tanimoto et al. (Cancer Research, 1997 Vol. 57:2884-2887) [Applicants reference A63].

Claims 12-14 are drawn to a method for diagnosing a cancer in a mammal, comprising detecting and measuring hepsin mRNA transcript in a biological subject from a region that is cancerous and comparing the hepsin mRNA transcript to a control, wherein the biological subject is selected from ovarian, prostate, breast, or lung tissue and wherein the data is stored electronically or in a paper format.

Tanimoto et al. disclose the identification of overexpressed hepsin in ovarian carcinomas compared to normal ovaries from patients (see Abstract). Tanimoto et al. disclose fresh ovarian tissue samples from surgical specimens were obtained from patients and used in Northern blots in which hepsin mRNA transcripts were overexpressed in carcinoma vs. normal tissues (see

Figure 1 and Table 1). The data of Tanimoto et al. is stored in the Cancer Research Journal in paper format.

Therefore, Tanimoto et al. anticipate claims 12-14.

Claims 33-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Zacharski et al. (Thromb Haemost, 1998 Vol. 79:876-877) [Applicants reference A72].

Claims 33-35 are drawn to a method for diagnosing a cancer in a mammal, comprising detecting hepsin protein expression in a biological subject from a region that is cancerous with an anti-hepsin antibody and comparing the hepsin protein expression to a control, wherein the biological subject is selected from ovarian, prostate, breast, or lung tissue and wherein the data is stored electronically or in a paper format.

Zacharski et al. disclose immunohistochemical techniques using purified polyclonal monospecific anti-hepsin antibodies to study hepsin expression in renal cell carcinoma and normal renal tissues *in situ* (see page 876, second column, last paragraph and Figure 1). Zacharski et al. further disclose staining of normal tissue and other tumor types, including ovarian cancer, adenocarcinoma and squamous cell carcinoma of the lung (see page 877, first column). The data of Zacharski et al. is stored in the Thromb Haemost Journal in paper format.

Therefore, Zacharski et al. anticipate claims 33-35.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221. The examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 746-8693.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

tcg
January 8, 2004

KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER